

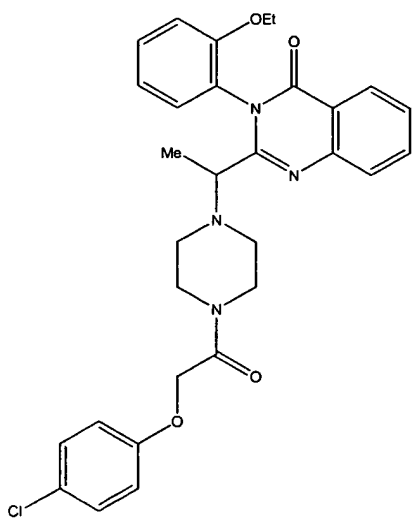
What is claimed:

1. A method of identifying an agent that is selectively toxic to human tumorigenic cells, comprising:
  - 5 (a) contacting test cells, which are engineered human tumorigenic cells, with a candidate agent;
  - (b) determining viability of test cells contacted in (a) with the candidate agent; and
  - 10 (c) comparing the viability of test cells determined in (b) with an appropriate control,wherein if the viability of the test cells is less than that of the control cells, then an agent that is selectively toxic to engineered human tumorigenic cells is identified.
- 15 2. A method of identifying an agent that is toxic to human tumorigenic cells, comprising:
  - (a) contacting test cells, which are engineered human tumorigenic cells, with a candidate agent;
  - (b) determining viability of test cells contacted in (a) with the candidate agent; and
  - 20 (c) comparing the viability of test cells determined in (b) with an appropriate control,wherein if the viability of the test cells is less than that of the control cells, then an agent that is toxic to engineered human tumorigenic cells is identified.
- 25 3. The method of claim 1, comprising further assessing, in an appropriate animal model, the selective toxicity to tumorigenic cells of the agent that is identified.
- 30 4. The method of claim 1, wherein the engineered human tumorigenic cells are selected from the group consisting of: (a) BJ-TERT cells, (b) BJ-

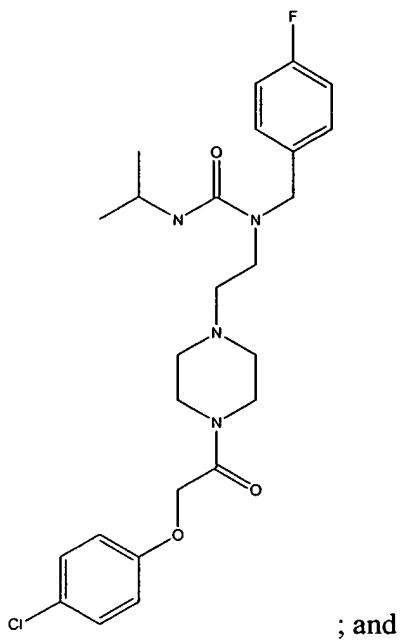
TERT/LT/ST cells, (c) BJ-TERT/LT/ST/RAS<sup>V12</sup> cells, (d) BJ-TERT/LT/RAS<sup>V12</sup>/ST cells, (e) TIP5/TERT cells, (f) TIP5/TERT/LT cells, (g) TIP5/TERT/LT/ST cells, (h) TIP5/TERT/LT/ST/RAS<sup>V12</sup> cells, (i) TIP5/TERT/E6 cells, (j) TIP5/TERT/E6/E7 cells, (k) TIP5/TERT/E6/E7/ST cells, and (l) TIP5/TERT/E6/E7/ST/RAS<sup>V12</sup> cells.

- 5
5. The method of claim 1, wherein the candidate agent is selected from the group consisting of: an annotated compound library, a National Cancer Institute diversity set of compounds, and a combinatorial library.
- 10
6. A method of producing an agent that is selectively toxic to human tumorigenic cells, comprising synthesizing an agent identified by the method claim 1.
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7. A method of inducing death in tumor cells, comprising contacting the cells with a compound selected from the group consisting of:

(a) a compound having the following formula:



(b) a compound having the following formula:

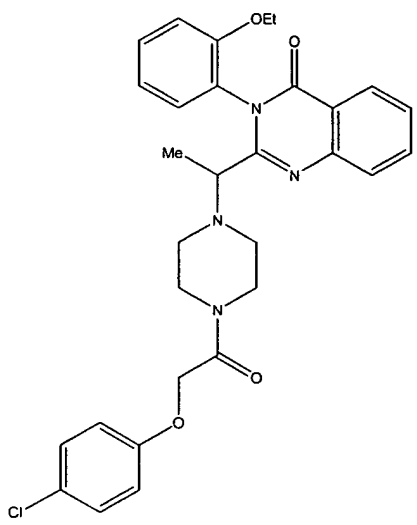


(c) a compound that is an analog of (a) and is selectively toxic to tumor cells.

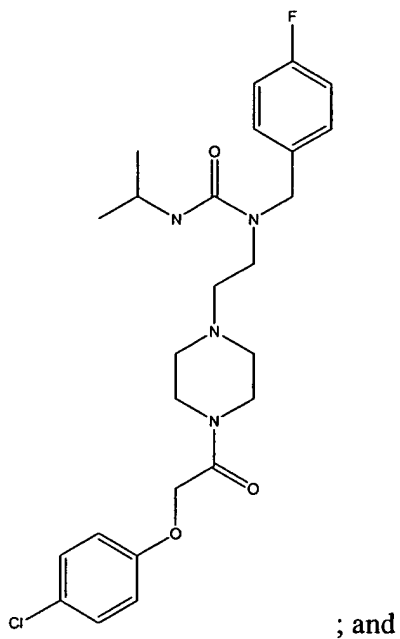
- 5 8. A method of inducing death in cells in which the RAS pathway is activated, comprising contacting the cells with a compound selected from the group consisting of:

(a) a compound having the following formula:

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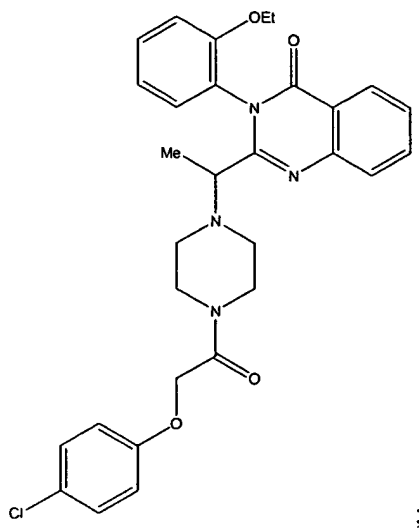


(b) a compound having the following formula:

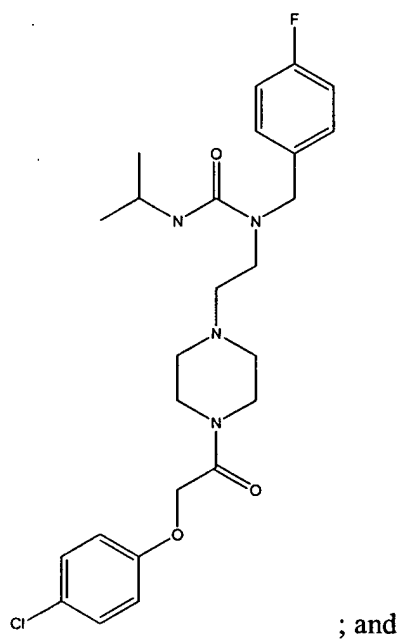


- 5 (c) a compound that is an analog of (a) and is selectively toxic to cells in which the RAS pathway is activated.
9. A method of inducing death in human cells expressing SV40 small T oncoprotein and oncogenic HRAS, comprising contacting the human cells
- 10 with a compound selected from the group consisting of:

(a) a compound having the following formula:



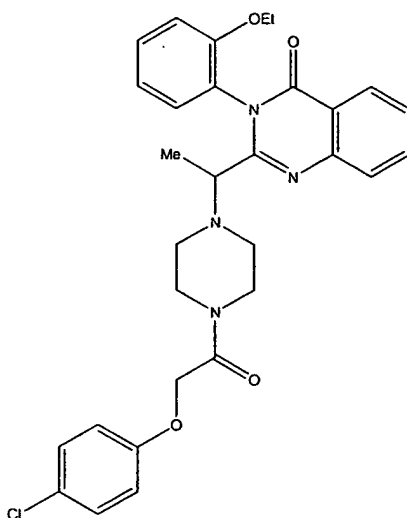
(b) a compound having the following formula:



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(c) a compound that is an analog of (a) and is selectively toxic to human cells expressing SV40 small T oncoprotein and oncogenic HRAS.

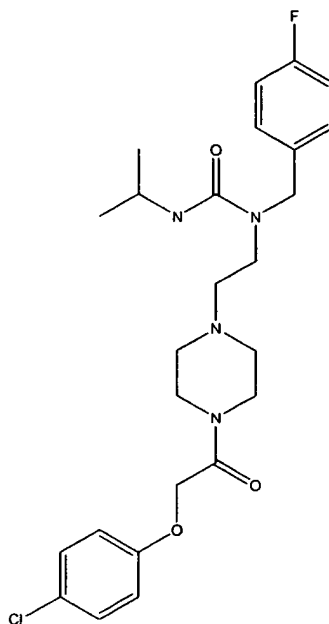
10. A compound having the following formula:



or an analog thereof, which is selectively toxic to engineered human tumorigenic cells.

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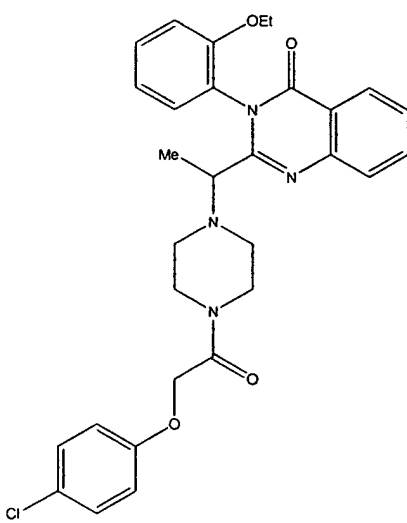
11. The compound of claim 10, wherein the compound is formulated with a pharmaceutically acceptable carrier.
12. A compound having the following formula:



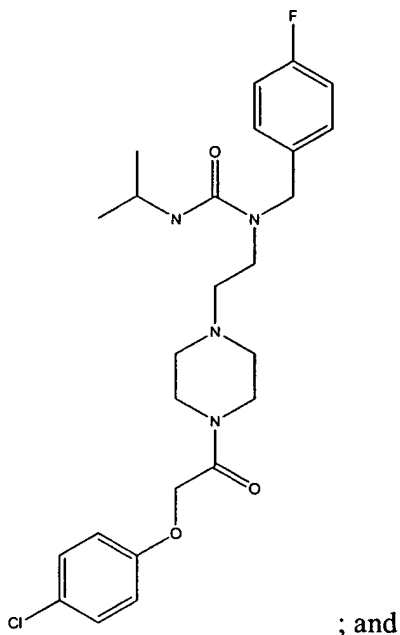
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or an analog thereof, which is selectively toxic to engineered human tumorigenic cells.

13. The compound of claim 12, wherein the compound is formulated with a pharmaceutically acceptable carrier.
14. A method of treating or preventing cancer in an individual, comprising administering to the individual a therapeutically effective amount of an agent identified by the method of claim 1.
15. The method of claim 14, wherein the cancer is characterized by cells in which the RAS pathway is activated.
16. The method of claim 14, wherein the cancer is characterized by cells expressing SV40 small T oncoprotein; oncogenic HRAS; or SV40 small T oncoprotein and oncogenic HRAS.
17. The method of claim 14, wherein the agent is selected from the group consisting of:
- (a) a compound having the following formula:



(b) a compound having the following formula:



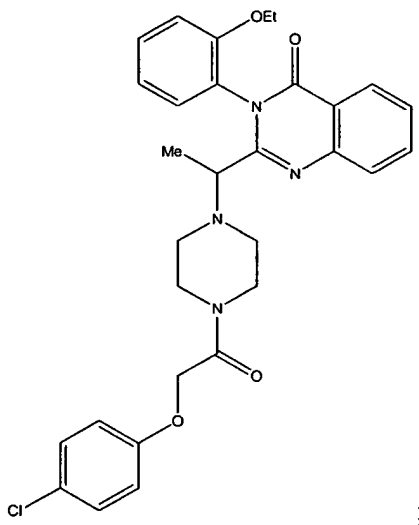
- 5 (c) a compound that is an analog of (a) and is selectively toxic to engineered human tumorigenic cells.
18. The method of claim 14, further comprising administering to the individual at least one additional anti-tumor agent that inhibits growth of the tumor cells in an additive or synergistic manner with the first agent.
- 10 19. A method of treating or preventing cancer in an individual, comprising administering to the individual a therapeutically effective amount of an agent identified by the method of claim 2.
- 15 20. The method of claim 19, wherein the cancer is characterized by cells in which the RAS pathway is activated.
21. The method of claim 19, wherein the cancer is characterized by cells expressing SV40 small T oncoprotein; oncogenic HRAS; or SV40 small T oncoprotein and oncogenic HRAS.
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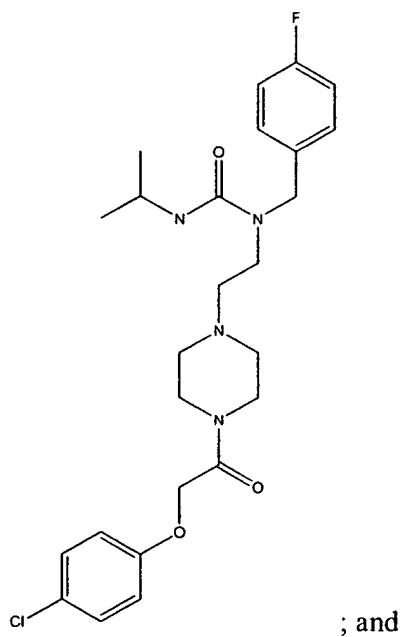
22. The method of claim 19, wherein the agent is selected from the group consisting of :

(a) a compound having the following formula:

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(b) a compound having the following formula:



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(c) a compound that is an analog of (a) and is selectively toxic to engineered human tumorigenic cells.

5 23. The method of claim 19, further comprising administering to the individual at least one additional anti-tumor agent that affects growth of the tumor cells in an additive or synergistic manner with the first agent.

24. A method of identifying a cellular component involved in tumorigenesis, comprising:

10 (a) contacting a cell with erastin; and

(b) identifying a cellular component that interacts with erastin, wherein the cellular component that is identified is a cellular component involved in tumorigenesis.

15 25. The method of claim 24, wherein the cellular component that interacts with erastin is one that interacts directly with erastin.

26. The method of claim 24, wherein the cellular component that interacts with erastin is one that interacts indirectly with erastin.

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27. The method of claim 24, wherein the cell is an engineered human tumorigenic cell.

25 28. A method of identifying a cellular component that interacts with erastin, comprising:

(a) contacting a cell with erastin; and

(b) identifying a cellular component that interacts with erastin, wherein the cellular component that is identified is a cellular component that interacts with erastin.

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29. The method of claim 28, wherein the cellular component that interacts with erastin is one that interacts directly with erastin.

30. The method of claim 28, wherein the cellular component that interacts with erastin is one that interacts indirectly with erastin.
- 5 31. The method of claim 28, wherein the cell is an engineered human tumorigenic cell.
32. A method of identifying a cellular component involved in tumorigenesis, comprising:
- 10 (a) contacting a cell with an inhibitor of erastin and contacting a cell with erastin; and
- (b) identifying a cellular component that interacts with the inhibitor in (a),
- wherein the cellular component that is identified is a cellular component involved in tumorigenesis.
- 15
33. The method of claim 32, wherein the cellular component that interacts with the inhibitor of erastin is one that interacts directly with the inhibitor of erastin.
- 20
34. The method of claim 32, wherein the cellular component that interacts with the inhibitor of erastin is one that interacts indirectly with the inhibitor of erastin.
- 25 35. The method of claim 32, wherein the cell is an engineered human tumorigenic cell.
36. A method of identifying a cellular component that interacts with erastin, comprising:
- 30 (a) contacting a cell with an inhibitor of erastin and contacting a cell with erastin; and

(b) identifying a cellular component that interacts with the inhibitor  
in (a),

wherein the cellular component that is identified is a cellular component that  
interacts with erastin.

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37. The method of claim 36, wherein the cellular component that interacts with  
erastin is one that interacts directly with erastin.

38. The method of claim 36, wherein the cellular component that interacts with  
10 erastin is one that interacts indirectly with erastin.

39. The method of claim 36, wherein the cell is an engineered human  
tumorigenic cell.

15 40. A method of identifying an agent that interacts with a cellular component  
involved in tumorigenesis, comprising:

(a) contacting a cell with erastin;

(b) identifying a cellular component that interacts with erastin;

(c) contacting a cell with a candidate agent; and

20 (d) identifying an agent that interacts with the cellular component in  
(b),

wherein the agent that interacts with the cellular component is identified as  
an agent that interacts with a cellular component involved in tumorigenesis.

25 41. The method of claim 40, wherein the cellular component that interacts with  
the candidate agent is one that interacts directly with the candidate agent.

42. The method of claim 40, wherein the cellular component that interacts with  
the candidate agent is one that interacts indirectly with the candidate agent.

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43. The method of claim 40, wherein the cell is an engineered human  
tumorigenic cell.

44. A method of producing an agent that interacts with a cellular component involved in tumorigenesis, comprising synthesizing an agent identified by the method of claim 40.
- 5
45. A method of identifying an agent that interacts with a cellular component that interacts with erastin, comprising:
- (a) contacting a cell with erastin;
  - (b) identifying a cellular component that interacts with erastin;
  - 10 (c) contacting a cell with a candidate agent; and
  - (d) identifying an agent that interacts with the cellular component in (b),
- wherein the agent that interacts with the cellular component is identified as an agent that interacts with a cellular component that interacts with erastin.
- 15
46. The method of claim 45, wherein the cellular component that interacts with the candidate agent is one that interacts directly with the candidate agent.
47. The method of claim 45, wherein the cellular component that interacts with the candidate agent is one that interacts indirectly with the candidate agent.
- 20
48. The method of claim 45, wherein the cell is an engineered human tumorigenic cell.
- 25
49. A method of producing an agent that interacts with a cellular component that interacts with erastin, comprising synthesizing an agent identified by the method of claim 45.
50. A method of identifying an agent that induces death in tumor cells by a non-apoptotic mechanism, comprising:
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- (a) contacting test cells with a candidate agent that induces death in tumor cells;

- (b) assessing whether the agent in (a) induces apoptosis in test cells;  
and  
(c) comparing induction of apoptosis in cells in (b) with an  
appropriate control,
- 5 wherein if apoptosis is induced in control cells but not in test cells, then an  
agent that induces death in tumor cells by a non-apoptotic mechanism is  
identified.
51. A method of producing an agent that induces death in tumor cells by a non-  
10 apoptotic mechanism, comprising synthesizing an agent identified by the  
method of claim 50.
52. The method of claim 50, wherein the tumor cell is an engineered human  
tumorigenic cell.
- 15 53. A method of conducting a drug discovery business, comprising:  
(a) by the method claim 40, identifying an agent that interacts with a  
cellular component that interacts with erastin;  
(b) assessing the efficacy and toxicity of an agent identified in (a), or  
20 analogs thereof, in animals; and  
(c) formulating a pharmaceutical preparation including one or more  
agents assessed in (b).
54. The method of claim 53, further comprising establishing a distribution  
25 system for distributing the pharmaceutical preparation for sale, and may  
optionally include establishing a sales group for marketing the  
pharmaceutical preparation.
55. A method of conducting a proteomics business, comprising:  
30 (a) by the method of claim 40, identifying an agent that interacts with  
a cellular component that interacts with erastin; and

(b) licensing, to a third party, the rights for further drug development of agents that interact with a cellular component that interacts with erastin.

- 5     56.     A method of conducting a drug discovery business, comprising:
- (a) by the method of claim 45, identifying an agent that interacts with  
              a cellular component that interacts with erastin;
- (b) assessing the efficacy and toxicity of an agent identified in (a), or  
              analogous thereof, in animals; and
- 10           (c) formulating a pharmaceutical preparation including one or more  
              agents assessed in (b).
57.     The method of claim 56, further comprising establishing a distribution  
              system for distributing the pharmaceutical preparation for sale, and may  
15           optionally include establishing a sales group for marketing the  
              pharmaceutical preparation.
58.     A method of conducting a proteomics business, comprising:
- (a) by the method of claim 45, identifying an agent that interacts with  
20           a cellular component that interacts with erastin; and
- (b) licensing, to a third party, the rights for further drug development  
              of agents that interact with a cellular component that interacts with  
              erastin.
- 25     59.     A method of conducting a drug discovery business, comprising:
- (a) by the method of claim 1, identifying an agent that is selectively  
              toxic to engineered human tumorigenic cells;
- (b) assessing the efficacy and toxicity of an agent identified in (a), or  
              analogous thereof, in animals; and
- 30           (c) formulating a pharmaceutical preparation including one or more  
              agents assessed in (b).

60. The method of claim 59, further comprising establishing a distribution system for distributing the pharmaceutical preparation for sale, and may optionally include establishing a sales group for marketing the pharmaceutical preparation.

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61. A method of conducting a proteomics business, comprising:  
(a) by the method of claim 1, identifying an agent that is selectively toxic to engineered human tumorigenic cells; and  
(b) licensing, to a third party, the rights for further drug development of agents that interact with a cellular component that interacts with erastin.

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62. A method of conducting a drug discovery business, comprising:  
(a) by the method of claim 2, identifying an agent that is toxic to engineered human tumorigenic cells;  
(b) assessing the efficacy and toxicity of an agent identified in (a), or analogs thereof, in animals; and  
(c) formulating a pharmaceutical preparation including one or more agents assessed in (b).

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63. The method of claim 62, further comprising establishing a distribution system for distributing the pharmaceutical preparation for sale, and may optionally include establishing a sales group for marketing the pharmaceutical preparation.

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64. A method of conducting a proteomics business, comprising:  
(a) by the method of claim 2, identifying an agent that is toxic to engineered human tumorigenic cells; and  
(b) licensing, to a third party, the rights for further drug development of agents that interact with a cellular component that interacts with erastin.

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65. A packaged pharmaceutical comprising: (i) a therapeutically effective amount of an agent identified by the method of claim 1; and (ii) instructions and/or a label for administration of the agent for the treatment of patients having cancer.

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66. A packaged pharmaceutical comprising: (i) a therapeutically effective amount of an agent identified by the method of claim 2; and (ii) instructions and/or a label for administration of the agent for the treatment of patients having cancer.

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